Rejection of Claims 21-24 Under 35 U.S.C. §112, first paragraph

Claims 21-24 stand rejected under 35 U.S.C. §112, first paragraph as allegedly lacking written description. Applicants respectfully request withdrawal of the rejection.

The Office Action asserts that variants of SEQ ID NOs:1-7 are not adequately described in the specification. The standard for written description whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, the Applicant was in possession of the invention as now claimed. *See Vas-Cath, Inc. v. Mahurkar*, 19 U.S.P.Q.2d 1111, 1117 (Fed. Cir. 1991). An Applicant shows possession of the claimed invention with all of its limitations using such descriptive words, structures, figures, diagrams, and formulas that fully set forth the claimed invention.

Given the specification, one of skill in the art would recognize that the Applicants were in possession of an isolated polypeptide selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7 and variants thereof.

The specification teaches that: "[p]olypeptides that do not comprise 100% identity to a polypeptide sequence shown in SEQ ID NOs:1-7 are considered 'variants'" and that "the invention provides polypeptides having at least 85% identity, more preferably at least 90% identity, and still more preferably at least 96%, 97%, 98%, or 99% identity to a polypeptide sequence shown in SEQ ID NOs:1-7." See page 5, lines 8-13.

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The specification goes on to define the meaning of "identity" and explains that sequences are aligned for identity calculations using a mathematical algorithm. See page 6, line 3 through page 7, line 5. The specification furthermore provides guidance concerning how to make phenotypically silent amino acid substitutions. See page 7, line 14 through page 8, line 20.

The specification also specifies that :

> Polypeptides of the invention specifically bind to an anti-Ehrlichia antibody. In this context "specifically binds" means that the polypeptide recognizes and binds to an anti-Ehrlichia antibody, but does not substantially recognize and bind other molecules in a test sample. See page 9, lines 8-11.

The specification also teaches how to screen a variant polypeptide to determine whether it binds to an anti-*Ehrilichia* antibody. See, e.g., page 18, line 19 through page 19, line 13.

Therefore, the specification teaches that a variant polypeptide of the invention has at least 85% identity, more preferably at least 90% identity, and still more preferably at least 96%, 97%, 98%, or 99% identity to a polypeptide sequence shown in SEQ ID NOs:1-7 and that it specifically binds to an anti-*Ehrlichia* antibody. One of skill in the art would recognize that variations can be made in a polypeptide shown in SEQ ID NOs:1-7 without affecting antigenicity. See specification page 8, lines 9-20 (teaching that proteins are surprisingly tolerant of amino acid substitutions and providing guidance to the types of amino acid substitutions that are well tolerated). Furthermore, one of skill in the art would recognize that the Applicants were in possession of polypeptides having

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a certain percentage sequence identity to SEQ ID NOs:1-7 and that also specifically bind an anti-*Ehrlichia* antibody.

Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 21-24 Under 35 U.S.C. §112, first paragraph

Claims 21-24 stand rejected under 35 U.S.C. §112, first paragraph as allegedly lacking enablement. Applicants respectfully request withdrawal of the rejection.

The Office Action asserts that variants of polypeptides shown in SEQ ID NOs:1-7 are not adequately enabled by the specification. Under 35 U. S. C. § 112, all that is required is that the specification describe the invention in such terms as to enable a person skilled in the art to make and use the invention. Thus, the specification must teach one skilled in the art how to make and use a variant of a polypeptide shown in SEQ ID NOs:1-7. The test of enablement is whether one reasonably skilled in the art (1) could make and use the invention (2) from the disclosures in the patent coupled with information known in the art (3) without undue experimentation. *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988); *United States v. Telectronics, Inc.*, 857 F.2d 778 (Fed. Cir. 1988); M.P.E.P. § 2164.01. "The determination of what constitutes undue experimentation is a given case requires the application of a standard of reasonableness, having due regard of the nature of the invention and the state of the art." *In re Wa*nds, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988) (citing *Ansul Co. v. Uniroyal, Inc.*, 169 U.S.P.Q. 759, 762-63 (2d Cir. 1971).

The specification teaches that a variant polypeptide of the invention has at least 85% identity, more preferably at least 90% identity, and still more preferably at least

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96%, 97%, 98%, or 99% identity to a polypeptide sequence shown in SEQ ID NOs:1-7 and it specifically binds to an anti-*Ehrlichia* antibody. One of skill in the art could easily design and make a polypeptide that falls within the given percentage sequence identity and screen it for specific binding to an anti-*Ehrlichia* antibody. For example, in the case of SEQ ID NO:2, which is a 20 amino acid long polypeptide, a variant polypeptide having 85% identity would have only about 3 changed amino acids. One of skill in the art could easily design and make such a variant polypeptide given SEQ ID NO:2. Furthermore, one of skill in the art has guidance from the specification as to which 3 amino acids could be changed. For example, the specification teaches how to make phenotypically silent amino acid substitutions. See page 7, line 14 through page 8, line 20.

One of skill in the art can clearly make a polypeptide once the sequence was designed. Additionally, the specification teaches that a polypeptide can be made by, for example, conventional peptide synthesis or by recombinant techniques. See page 10, lines 6-13. One of skill in the art could then screen a variant polypeptide for binding to an anti-*Ehrlichia* antibody by the methods described in Example 1.

The law is well settled that the test of enablement "is not merely quantitative, since a considerable amount of experimentation is permissible, if it merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Wa*nds, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988) (citing *Ansul Co. v. Uniroyal, Inc.*, 169 U.S.P.Q. 759, 762-63 (2d Cir. 1971). One of skill in the art understands the meaning of sequence identity and

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most certainly could design and make a polypeptide sequence that has 85% or more sequence identity to SEQ ID NOs:1-7 using only routine experimentation. Once one of skill in the art had designed and made a variant polypeptide of the invention, they could use only routine screening to identify whether the polypeptide specifically binds to an anti-*Ehrlichia* antibody. Therefore, even though it could conceivably take a considerable amount of experimentation to design and make a variant polypeptide of the invention, such design and manufacture requires only routine experimentation that is well-known and understood to one of skill in the art. Additionally, the specification provides direction to guide one of skill in the art to the experimentation that is necessary to design, make and screen a variant polypeptide of the invention.

Finally, the specification teaches that a variant polypeptide can be used to detect the presence of anti-*Ehrlichia* antibodies. See page 11, line 22 through page 17, line 9. Therefore, one of skill in the art, given the specification could make and use the variant polypeptides of the invention without undue experimentation.

Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 21-24 Under 35 U.S.C. §102(a)

Claims 21-24 stand rejected under 35 U.S.C. §102(a) as allegedly anticipated by Waner *et al.* Applicants respectfully traverse the rejection.

Amended claim 21 recites a device containing one or more polypeptides selected from the group consisting of the polypeptides shown in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7. The polypeptides are 18-20 amino acids long and are derived from *Ehrlichia canis* and

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Ehrlichia chaffeensis. See specification page 6, Table 1. The use of these polypeptides provide higher sensitivity and specificity than enzyme-linked immunosorbent assays (ELISAs) and indirect immunofluorescense assays (IFA's) that use antigens such as infected cells, cell lysates or purified *Ehrlichia* proteins. See specification page 2, line 21-25 through page 3, line 2.

The Office Action asserts that the polypeptide-containing devices of the invention are inherently present in the assays reported in Waner. Waner teaches an IFA for *Ehrlichia canis* that uses DH82 cells that are heavily infected with *E. canis* as an antigen. See page 240, second column, last paragraph. Waner also teaches an ELISA for *E. canis* that uses an *E. canis* antigen derived from mouse J774.A1-infected cells. See page 241, first column, first full paragraph.

Initially, Waner does not teach or suggest the use of any types of *E. chaffeensis* polypeptides in a device. SEQ ID NOs: 3-7 of the present invention are *E. chaffeensis* polypeptides and therefore cannot be anticipated by Waner.

Additionally, Waner does not teach or suggest the use of distinct *E. canis* polypeptides as shown in SEQ ID NOs:1-2. Rather, Waner teaches the use of *E. canis* infected cells or an antigen purified from *E. canis* infected cells in the disclosed assays. Therefore, Waner does not teach, suggest, or inherently disclose the specific, individual polypeptides shown in SEQ ID NOs:1-2 and does not identify the polypeptide fragments to be of any particular diagnostic use. There is no teaching in Waner, directly or inherently, that would direct one of skill in the art to the particular defined sequences of SEQ ID NOs:1-2 for any reason. Warner does not teach or suggest that SEQ ID NOs:1-2

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are sequences that would be useful as individual peptides apart from entire *E. canis* infected cells or proteins. Warner provides no recognition or suggestion that the distinct polypeptides shown in SEQ ID NOs:1-2 or any other polypeptide fragments would be of diagnostic use.

Waner does not anticipate claims 21-24 because Waner does not teach, suggest, or inherently disclose each and every element of claims 21-24. Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 21-24 Under 35 U.S.C. §102(b)

Claims 21-24 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Cadman *et al.* Applicants respectfully traverse the rejection.

The Office Action asserts that the polypeptide-containing devices of the invention are inherently present in the assays disclosed in Cadman. Cadman teaches an IFA for *Ehrlichia canis* that uses DH82 cells which are heavily infected with *E. canis* as an antigen. See Cadman, first column, fourth paragraph. Cadman also teaches a dot-blot enzyme linked immunoassay (DBELIA) for *E. canis* that uses an *E. canis* antigen purified from infected DH82 cells. See Cadman, first column, fifth paragraph.

Initially, Cadman does not teach or suggest the use of any type of *E. chaffeensis* polypeptides in a device. SEQ ID NOs: 3-7 of the present invention are *E. chaffeensis* polypeptides and therefore cannot be anticipated by Cadman.

Additionally, Cadman does not teach or suggest the use of distinct *E. canis* polypeptides as shown in SEQ ID NOs:1-2. Rather, Cadman teaches the use of *E. canis* infected cells or an antigen purified from *E. canis* infected cells in the disclosed assays.

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Therefore, Cadman does not teach, suggest, or inherently disclose the specific, individual polypeptides shown in SEQ ID NOs:1-2 and does not identify the polypeptide fragments to be of any particular diagnostic use. There is no teaching in Cadman, directly or inherently, that would direct one of skill in the art to the particular, defined sequences of SEQ ID NOs:1-2 for any reason. Cadman does not teach or suggest that SEQ ID NOs:1-2 are sequences that would be useful as individual peptides apart from entire *E. canis* infected cells or proteins. Cadman provides no recognition or suggestion that the distinct polypeptides shown in SEQ ID NOs:1-2 or any other polypeptide fragments would be of diagnostic use.

Cadman does not anticipate claims 21-24 because Cadman does not teach, suggest, or inherently disclose each and every element of claims 21-24. Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 21-24 Under 35 U.S.C. §102(b)

Claims 21-24 stand rejected under 35 U.S.C. §102(a) as allegedly anticipated by Zhi *et al.* Applicants respectfully traverse the rejection.

The Office Action asserts that the polypeptide-containing devices of the invention are inherently present in the assays reported in Zhi. Initially, Zhi teaches assays for the detection of Human Granulocytic Ehrlichiosis Agent (HGE). HGE is closely related to or identical to *E. equi* and *E. phagocytophilia*. See CDC Publication, "Human Ehrilichioisis in the United States;" Dumler *et al.*, Int. J. Syst. Evol. Microbiol. 51:2145 (2001) (abstract) (copies attached). Therefore, Zhi does not teach or suggest *E. canis* or *E. chaffeensis* antigens, proteins or polypeptides contained within a device.

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However, in the event that the HGE taught in Zhi could be considered to be *E. canis* or *E. chaffeensis*, Zhi would still not teach or suggest each and every element of claims 21-24.

Zhi teaches Western immunoblot analysis and dot immunoblot assays for HGE that uses HGE rP44, a 35kDa fusion protein, or purified HGE organisms as assay antigens. See page 1668, first column, first and second full paragraphs; page 1668, second column, first full paragraph.

Zhi does not teach or suggest the use of distinct *E. canis* and *E. chaffeensis* polypeptides as shown in SEQ ID NOs:1-7. Rather, Zhi teaches the use of HGE rP44 or purified HGE organisms in the disclosed assays. Therefore, Zhi does not teach, suggest, or inherently disclose the specific, individual polypeptides shown in SEQ ID NOs:1-7 and does not identify the polypeptide fragments to be of any particular diagnostic use. There is no teaching in Zhi, directly or inherently, that would direct one of skill in the art to the particular, defined sequences of SEQ ID NOs:1-7 for any reason. Zhi does not teach or suggest that SEQ ID NOs:1-7 are sequences that would be useful as individual peptides apart from entire HGE organisms or HGE rP44. Zhi provides no recognition or suggestion that the distinct polypeptides shown in SEQ ID NOs:1-7 would be of diagnostic use.

Zhi does not anticipate claims 21-24 because Zhi does not teach, suggest, or inherently disclose each and every element of claims 21-24. Applicants respectfully request withdrawal of the rejection.

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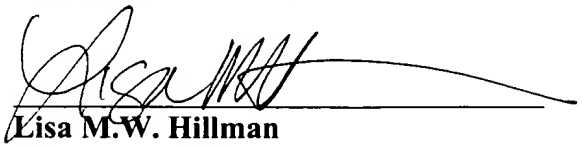
Applicants respectfully request the withdrawal of all rejections and the speedy allowance of the claims.

Respectfully submitted,

Date: June 19, 2002 By: 

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MARKED-UP VERSION OF CLAIMS TO SHOW CHANGES MADE

22. (Amended) The device of claim 21, further comprising instructions for use of the one or more polypeptides for the identification of an [Ehrlichia] *Ehrlichia* infection in a mammal.

23. (Amended) The device of claim 22, wherein the identification of an [Ehrlichia] *Ehrlichia* infection is done using a method of detecting presence of antibodies to [Ehrlichia] *Ehrlichia* comprising:

(a) contacting one or more polypeptides selected from the group consisting of the polypeptides shown in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, and variants thereof, with a test sample suspected of comprising antibodies to [Ehrlichia] *Ehrlichia*, under conditions that allow polypeptide/antibody complexes to form;

(b) detecting polypeptide/antibody complexes;

wherein the detection of polypeptide/antibody complexes is an indication that an [Ehrlichia] *Ehrlichia* infection is present.

24. (Amended) The device of claim 22, wherein the [Ehrlichia] *Ehrlichia* infection is caused by *Ehrlichia canis* or *Ehrlichia chaffeensis*.

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1645

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 00-1278)

In re Application of:)
)
Lawton, et al.)
)
Serial No.: 09/765,739) Examiner: V. Ford
)
Filed: January 18, 2001) Art Unit: 1645
)
For: Compositions and Methods for Detection)
Of Ehrlichia Canis and Ehrlichia)
Chaffeensis Antibodies)

TRANSMITTAL LETTER

Asst. Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

In regard to the above identified application,

1. We are transmitting herewith the attached:
   a) Response to Office Action dated April 8, 2002;
   b) Return postcard

2. With respect to fees:
   a) It is believed no fee is due at this time.
   b) Please charge any underpayment or credit any overpayment our Deposit Account, No. 13-2490.

3. GENERAL AUTHORIZATION: Please charge any additional fees or credit overpayment to Deposit Account No. 13-2490. A duplicate copy of this sheet is enclosed.

4. CERTIFICATE OF MAILING UNDER 37 CFR § 1.8: The undersigned hereby certifies that this Transmittal Letter and the paper, as described in paragraph 1, are being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to the Asst. Commissioner for Patents, Washington, D.C. 20231 on June 19, 2002.

Respectfully submitted,

Date: June 19, 2002

Lisa M.W. Hillman
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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 00-1278)

In re Application of:

Lawton, et al.

Serial No.: 09/765,739

Filed: January 18, 2001

For: Compositions and Methods for Detection Of Ehrlichia Canis and Ehrlichia Chaffeensis Antibodies

Examiner: V. Ford

Art Unit: 1645

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Asst. Commissioner for Patents
Washington, D.C. 20231

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Date: June 19, 2002

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